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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/663,533	09/16/2003	Adam M. Gilbert	AM100279/WYNC-0677	3576

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EXAMINER	
HUANG, EVELYN MEI	
ART UNIT	**PAPER NUMBER**
1625	

DATE MAILED: 04/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/663,533	GILBERT ET AL.	
	Examiner	Art Unit	
	Evelyn Huang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26 and 33-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26 and 33-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 26, 33-52 are pending. Claims 1-25, 27-32 have been canceled according to the preliminary amendment filed on 9-16-2-2003.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 26, 33-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 26, 'eating disorders', 'sexual dysfunction', 'disorders of thermoregulation', 'sleep dysfunction', and 'neurodegenerative diseases' are unclear since they are general classes of disorders embracing opposing and conflicting conditions. For example, 'eating disorder' would encompass both hyperphagia and anorexia, 'sexual dysfunction' would embrace the conditions involving both the inhibitory and stimulatory sexual behaviors, 'disorders of thermoregulation' would include hypothermia and hyperthermia, 'sleep dysfunction' would cover both insomnia and nacrolepsy etc. What are the intended metes and bounds of these disorders/conditions?

The rejection is applicable to all the claims dependent on claim 26.

Claim Rejections - 35 USC § 112(1)

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26, 33-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

a. *Nature of the invention.*

The instant invention is drawn to the method of using a benzo[1,4]dioxin-azabicyclo[3.2.1]octane compound in the treatment of neurodegenerative diseases, eating disorders, disorders of thermoregulation, sleep dysfunction, or sexual dysfunction.

b. *State of the prior art and the level of the skill in the art.*

5-HT receptors are known to have subclasses differing in their structures, regional distribution, pharmacology, modes of actions, and functions (Wijngaarden et al. Recl. Trav. Chim. Pays-Bas, 1993, 112:126-130; Barnes et al. Neuropharmacology, 1999, 38: 1083-1092, pages 1085-6). While $5HT_{1A}$ receptor has been implicated in many physiological responses, and $5HT_{1A}$ receptor agonist has been shown to have anxiological and antidepressant activity, the nexus between neurodegenerative diseases, eating disorders, disorders of thermoregulation, sleep dysfunction, or sexual dysfunction and $5HT_{1A}$ receptor has not been fully established. For example, while $5HT_{1A}$ receptor agonist evokes hypothermia, inhibition of 5HT synthesis and 5-HT lesions do not prevent hypothermia when the agonists are injected in rats (Barnes, page 1092). Some of the responses elicited by a $5HT_{1A}$ receptor agonist, 8-OH-PAT, such as hyperphagia (Fletcher et al. Psychopharmacology, 1990, 100(2): 188-94, abstract), altered sexual behavior (Matuszewich et al. Brain Research 1999, 820(1-2): 55-62, abstract), are not reversed by a $5HT_{1A}$ receptor antagonist, thereby suggesting that these effects are not mediated by the $5HT_{1A}$ receptor.

At present, there is no umbrella drug known to be effective in treating neurodegenerative diseases, eating disorders, disorders of thermoregulation, sleep dysfunction, and sexual dysfunction. It is the state of the art that there is no known cure or prevention for a neurodegenerative disease such as Alzheimer's disease. There are only four medications available in the United States available to temporarily slow the early stages of Alzheimer's disease. The current drugs for the treatment of Alzheimer's disease, Aricept, Exelon, Reminyl and Cognex, treat early stages of Alzheimer's disease by delaying the breakdown of

acetylcholine. Memantine, which blocks excess amounts of glutamate treats late stage Alzheimer's disease.
(URL:http://www.cnn.com/2003/HEALTH/conditions/09/24/alzheimers.drug.ap/index.html

The level of the skill in the 5-HT_{1A} receptor antagonist art is high.

c. *Predictability/unpredictability of the art.*

The high degree of unpredictability is well recognized in the 5-HT receptor ligand art. A slight change in the structure of the compound would drastically alter its affinity and selectivity (Wijngaarden, Recl. Trav. Chim. Pays-Bas, 1993, 112:126-130, pages 129-130, Fig. 6, Fig. 7, Fig. 8). The in vitro binding data do not necessarily reflect the in vivo activity.

d. *Amount of guidance/working examples.*

Preparation of example compounds has been described.

The procedures for the 5-HT transporter binding assays, 5-HT_{1A} receptor binding assays, and the assay for the assessment of the antagonist activity, are found on pages 9-10 of the specification. Results are shown for Examples 1-11 on page 11 of the specification.

No in vivo procedures are described.

e. *The breadth of the claims.*

Applicant's assertion that all the inventive compounds would be effective in treating any neurodegenerative disease (arising from different origins involving different mechanisms), any eating disorder (including the conflicting hyperphagia and anorexia), any disorder of thermoregulation (including the opposing hypothermia and hyperthermia), any sleep dysfunction (including the conflicting insomnia and narcolepsy) or any sexual dysfunction (including the conditions involving the opposing inhibitory and stimulatory sexual behaviors) does not commensurate with the scope of the objective enablement, especially in view of the high degree of unpredictability in the art, the limited working examples and the non-establishment of the nexus between the antagonism of $5HT_{1A}$ receptor and the recited disorders (paragraphs b, c, d above).

f. *Quantitation of undue experimentation.*

Since the instant 'neurodengerative disorders' 'eating disorders', 'disorders of thermoregulation', 'sleep dysfunction', and 'sexual dysfunction' etc. are general classes of disorders embracing opposing and conflicting conditions arising from diverse origins, it is

impossible to use a single $5HT_{1A}$ receptor antagonist compound of the instant to treat all these contradictory disorders (see paragraph 2 above). Furthermore, in view of the high degree of unpredictability in the art, the limited working examples and the fact that the breadth of the claims does not commensurate with that of the objective enablement and the nexus between the antagonism of $5HT_{1A}$ receptor and the recited disorders has not been fully established, the disclosure as presented would not allow one of ordinary skill in the art to use the invention as claimed without undue experimentation (paragraphs b-e above).

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 26, 33-52 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 22-28 of U.S. Patent No. 6656951. Although the conflicting claims are not identical, they are not patentably distinct from each other. The instant method was part of the original claims in the parent application that matured into 6656950, and it is not a result of a restriction requirement of the parent application. The cognitive deficits in the patented method is also a neurodegenerative disease as recited in the instant.

Conclusion

5. No claims are allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is 571-272-0686. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Evelyn Huang
Primary Examiner
Art Unit 1625